Biol. Chem., 1987, Vol. 262(36):17556-62 ("Vann (b)") in combination with Staesche et al. J. Biol. Sci., 1997, Vol. 272(39):24313-24318 ("Staesche (a)") or Staesche et al. J. Biol. Sci., 1997, Vol. 272(39):24319-24324 ("Staesche (b)").

In support of the rejection, the Examiner relies upon Vann (a) and (b) as showing the basic steps of sialic acid biosynthesis, an appropriate cDNA clone therefore and the regulatory details. The Examiner concludes that due to the important industrial application, the skilled artisan would have been motivated to develop a method for manufacture of large amounts of sialic acid, and with a reasonable expectation of success.

This rejection is respectfully traversed. However, prior to setting forth their bases for traversal, Applicants would first like to discuss briefly the salient features of the present invention and, *inter alia*, its patentable nature over the prior art.

As the Examiner is aware, the present invention broadly relates to a process for producing N-acetylneuraminic acid utilizing N-acetylmannosamine, an energy source, and:

(1) a culture of a microorganism (or treated product) having N-acetylneuraminic acid aldolase and a culture of a microorganism (or treated product) capable of producing pyruvic acid,

(2) a culture of a microorganism (or treated product) having N-acetylneuraminic acid synthetase activity and a culture of a microorganism (or treated product) capable of producing phosphoenolpyruvic acid.

The present inventors determined, entirely unexpectedly, that N-acetylneuraminic acid can be efficiently produced from inexpensive materials by utilizing a microorganism which is capable of producing pyruvic (or phosphoenolpyruvic) acid, and the present invention has been completed based on this finding (see in the specification from page 2, line 35 to page 3, line 4).

These features are simply not addressed by the prior art, even taken in combination.

As relied upon by the Examiner, Vann (a) teaches that N-acetylneuraminic acid (NANA) synthetase catalyzes the formation of NANA as indicated by its coupling to the CMP-NeuAc synthetase reaction. Vann (a) also teaches NANA synthetase condenses mannosamine and phosphoenolpyruvic acid (PEP) but CMP-NeuAc synthetase does not.

However, Vann (a) does not teach or suggest anything concerning production of N-acetylneuraminic acid utilizing a microorganism capable of producing pyruvic acid or phosphoenolpyruvic acid.

Vann (b) is cited only as teaching the purification, properties and genetic location of CMP-NeuAC synthetase in E. coli K1. However, CMP-NeuAc is not relevant to the subject matter of the pending claims.[1]

Accordingly, neither Vann (a) nor Vann (b) addresses the claimed features of the present invention, namely producing N-acetylneuraminic acid utilizing a microorganism which is capable of producing pyruvic or phosphoenolpyruvic acid. These deficiencies are simply not addressed by the secondary references to Staesche.

Staesche (a) teach that NANA biosynthesis is initiated by the action of UDP-N-acetylglucosamine 2-epimerase and N-acetylmannosamine kinase, and NANA formation starts by the conversion of UDP-N-acetylglucosamine to N-acetylmannosamine in the presence of an energy donor such as ATP.

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1 In that regard, CMP-NeuAc synthetase catalyzes the formation of CMP-NeuAc from NeuAc and CTP, and thus differs in kind from NAN synthetase recited in Applicants' claims.

Staesche (b) et al. confirms that NANA biosynthesis is regulated by UDP-N-acetylglucosamine 2-epimerase in rat liver cells.[2]

However, UDP-N-acetylglucosamine 2-epimerase does not relate to the process of the claimed invention.

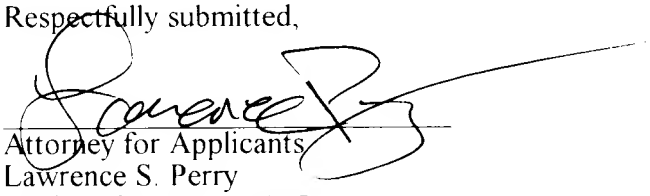
Thus, no prior art is relevant to, let alone teaches or suggests producing N-acetylneuraminic acid utilizing a microorganism which is capable of producing pyruvic acid or phosphoenolpyruvic acid. Accordingly, respectfully submitted, the Examiner has not made out a prima facie case of obviousness.

In view of the above remarks, Applicants earnestly submit that all of the Examiner's concerns are now overcome and the claims are now in allowable condition. Accordingly, reconsideration and allowance of this application is earnestly solicited.

Claims 1-18 remain presented for continued prosecution.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,



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[2] In this regard, Staesche's UDP-N-acetylglucosamine 2-epimerase catalyzes the formation of ManNAc from UDP-GlcNAc (see page 24313, right column, lines 7-9 of Staesche (a)) and thus differs in kind from N-acetylglucosamine 2-epimerase described in Applicants' claims.